IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

IN RE: GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS (GLP-1 RAs) PRODUCTS LIABILITY LITIGATION	:	**CIVIL ACTION**
THIS DOCUMENT RELATES TO:	:	**MDL No. 3094**
ALL ACTIONS / ALL CASES	:	**2:24-md-03094-KSM**

DEFENDANTS' JOINT RESPONSE IN OPPOSITION TO PLAINTIFFS' MOTION TO PARTIALLY EXCLUDE OPINIONS OF LINDA NGUYEN, M.D. UNDER RULE 702

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INTRODUCTION

Dr. Linda Nguyen is a leading authority on gastroparesis and co-author of the 2022 American College of Gastroenterology (ACG) Clinical Guideline on Gastroparesis. She opines that (1) symptoms associated with gastroparesis closely overlap with many other conditions; (2) a diagnosis of gastroparesis cannot be made based on clinical presentation alone; and (3) a reliable diagnosis of gastroparesis requires an objective gastric emptying study. *See* Nguyen Rpt., Ex. A, at 8.[1] Each of these opinions addresses the critical Issue 1 question: "whether gastroparesis may be reliably diagnosed in a clinical setting absent objective testing." CMO 18 at ¶¶ 4, 6 (Doc. 235).

Plaintiffs do not seek to exclude these opinions, which follow the guidelines of numerous leading U.S. and international organizations, as well as decades of research and clinical experience, and largely align with Plaintiffs' own expert testimony. They instead move to exclude tangential points immaterial to Issue 1: (1) Dr. Nguyen's "suggestion" that transient or non-chronic delayed gastric emptying is not "true" gastroparesis—a topic not part of Issue 1 so an opinion that she will not offer now; and (2) Dr. Nguyen's discussion of a study abstract that indicates that gastrointestinal symptoms are not correlated with delayed gastric emptying in GLP-1RA patients—an abstract that both of ***Plaintiffs'*** experts rely upon and that Dr. Nguyen properly discussed in rebuttal.

Plaintiffs are wrong, mischaracterize Dr. Nguyen's opinions, and raise points that distract from the actual Issue 1 before the Court. The Court should deny their Motion.

[1] All exhibits set forth in this Memorandum are attached to the March 31, 2025 Declaration of Lucas P. Przymusinski, M.D., J.D.

BACKGROUND

I. DR. NGUYEN'S QUALIFICATIONS.

Dr. Nguyen is a preeminent practitioner and scholar in the field of Neurogastroenterology and Motility disorders, with a focus on gastroparesis. Dr. Nguyen serves as the Interim Chief of Gastroenterology & Hepatology at Stanford Health Care and is a Clinical Professor at Stanford University. *See* Nguyen Rpt., Ex. A, at 1-2. Previously, she directed Stanford's Neurogastroenterology and Gastrointestinal Motility division for over a decade, transforming it into one of the largest gastrointestinal motility programs in the nation. *Id.* Her substantial research contributions include over 90 peer-reviewed publications and eight book chapters, primarily focusing on gastroparesis and similar disorders. *Id.*

Beyond her clinical and research practice, Dr. Nguyen holds prominent leadership positions in major gastroenterology societies, including serving as the current Vice Chair of the Clinical Practice Section for the American Gastroenterological Association (AGA). *Id.* She sits on the Board of Directors for the ACG Institute, is co-founder and co-chair of the American Neurogastroenterology and Motility Society (ANMS) Women in Neurogastroenterology Program, and contributes to the Neurogastroenterology and Motility Disorders of the Gastrointestinal Disorders section of the medical journal *Current Gastroenterology Reports*. *Id.* Dr. Nguyen's expertise has garnered national and international acclaim. In 2021, she was invited to co-author the ACG Clinical Guideline on Gastroparesis, which is the most current domestic clinical guideline addressing the diagnosis and management of gastroparesis. *Id.* And she was selected as one of the two U.S. delegates to contribute to the development of an international Consensus Statement on idiopathic gastroparesis (*i.e.*, gastroparesis of unknown cause). *Id.*

II. DR. NGUYEN'S OPINIONS.

Dr. Nguyen opines—and Plaintiffs' experts agree—that gastroparesis is a medical condition characterized by: (i) gastrointestinal symptoms (such as nausea, vomiting, abdominal pain, and early satiety); (ii) occurring without mechanical obstruction; and (iii) occurring in the presence of delayed gastric emptying. *See* Nguyen Rpt., Ex. A, at 8; Siegel Rpt., Ex. B, at 10; Raines Rpt., Ex. C, at 4. The symptoms associated with gastroparesis are non-specific. In other words, they overlap with symptoms of many other conditions, and result from a variety of different physiologic effects. Plaintiffs' experts agree here as well; these points are not in dispute. *See* Nguyen Rpt., Ex. A, at 3; Siegel Rpt., Ex. B, at 15; Raines Rpt., Ex. C, at 7-8.

Several studies, including Dr. Nguyen's own research, have shown that symptoms are a poor predictor of whether a patient suffers from delayed gastric emptying. Nguyen Rpt., Ex. A, at 3-4. Diagnoses without objective testing to confirm delayed gastric emptying result in a startling misdiagnosis rate, ranging from 30% (per Plaintiffs' own expert, Dr. Raines) to 80% (based on a published peer-reviewed study). *See* Raines Dep., Ex. I, at 282:2-12; Cangemi 2023, Ex. N, at 2671. These stark reliability problems apply to GLP-1RA patients. The sole data in the record on this front, as cited by both of Plaintiffs' experts, is a study abstract showing that even symptomatic GLP-1RA patients ***do not have delayed gastric emptying*** most of the time. *See* Lupianez-Merly 2024, Ex. P; Siegel Rpt., Ex. B, at 17; Raines Rpt., Ex. C, at 12. In the same vein, and based on the same Lupianez-Merly paper, Dr. Nguyen also observes that "[w]hile GI symptoms are quite common with GLP-1RAs, clinically delayed gastric emptying is relatively rare." Nguyen Rpt., Ex. A, at 17.

Recognizing the ubiquity of non-specific gastrointestinal symptoms, even in patients without delayed gastric emptying, clinical guidelines consistently stress the need for a gastric emptying study or other objective testing to reliably diagnose gastroparesis. These authorities

include the 2022 ACG Clinical Guideline, which offers a standardized nationwide approach for healthcare providers in reliably diagnosing and treating gastroparesis. *See* Nguyen Dep., Ex. D, at 63:5-9; Camilleri 2022, Ex. J. Likewise, in 2021, the United European Gastroenterology and the European Society of Neurogastroenterology and Motility issued guidelines concluding that an "abnormal [gastric emptying] test is mandatory for establishing a diagnosis of gastroparesis." Schol 2021, Ex. E, at 293. In 2022, the AGA issued a clinical practice update on the management of medically refractory gastroparesis, recommending to "verify appropriate methodology of the gastric emptying study to ensure an accurate diagnosis of delayed gastric emptying." Lacy 2022, Ex. F, at 491. And, in 2025, a consensus group made up of major international neurogastroenterology and motility societies explained that "symptoms of gastroparesis lack specificity" and that "a demonstration of delayed gastric emptying is necessary for diagnosis." Schol 2025, Ex. G, at 70. Plaintiffs' motion itself cites a number of studies or authorities reaching similar conclusions.[2]

[2] *See, e.g.*, Mot. 7 (citing Patrick 2008, Pls. Ex. F, at 728 ("Consequently, the diagnosis [of gastroparesis] is restricted to patients with chronic nausea and vomiting who have normal foregut imaging but ***objective evidence*** of profound delay in gastric emptying.") (emphasis added); Camilleri 2011, Pls. Ex. G, at 7 ("Gastroparesis is diagnosed by demonstrating delayed gastric emptying. . . . The current diagnostic method of choice is scintigraphic measurement of the emptying of solids"); Kim 2019, Pls. Ex. H, at 30 ("[M]otility abnormality should be assessed using various tests, including gastric emptying test and manometry."); Camilleri 2012, Pls. Ex. I, at 598 ("[I]n such patients with symptoms suggesting gastroparesis, it is important to investigate with tests of gastric emptying of solids."); Stein 2015, Pls. Ex. J, at 550 ("The diagnosis of GP is made using a combination of characteristic symptoms in conjunction with objective evidence of delayed gastric emptying in the absence of mechanical obstruction."); Tack 2014, Pls. Ex. K, at 469 ("The next step in diagnosing gastroparesis is measurement of the gastric emptying rate. Scintigraphic assessment of disappearance of a radioisotope-labeled meal . . . is still considered the gold standard for measuring gastric emptying.").

ARGUMENT

I. WHETHER TRANSIENT DELAYED-GASTRIC EMPTYING SHOULD BE CALLED "GASTROPARESIS" IS NOT AT ISSUE HERE.

The Court should deny Plaintiffs' motion to exclude Dr. Nguyen's supposed "opinion" that drug effects on gastric emptying are not "true" gastroparesis. Regardless of whether Plaintiffs can accurately label transient delayed gastric emptying and gastrointestinal symptoms as "drug-induced gastroparesis" (Siegel Rpt., Ex. B, at 16; Raines Rpt., Ex. C, at 12), the question before the Court at Issue 1 is not whether the medicines could cause certain gastrointestinal symptoms in some patients. The medicines' labels clearly warn of such symptoms. Nor is the question whether certain forms of delayed gastric emptying are most accurately dubbed "gastroparesis" or something else. Many leading authorities, including Dr. Nguyen, conclude that the condition "gastroparesis" refers to specific types of clinical criteria and presentations that are indicative of a chronic disease. *See, e.g.*, Nguyen Rpt., Ex. A, at 16. But Dr. Nguyen acknowledges that some medications can delay gastric emptying and cause transient gastrointestinal symptoms—a condition that she acknowledges some doctors or authorities refer to as "iatrogenic gastroparesis" or "drug-induced gastroparesis." *See* Nguyen Dep., Ex. D, at 61:2-13. Critically, all leading authorities and Plaintiffs' experts agree that gastroparesis—whether drug-induced, temporary, chronic, or otherwise—requires delayed gastric emptying. As such, the present question is whether a physician can reliably diagnose gastroparesis of any kind without objective testing to confirm delayed gastric emptying is present.

Contrary to Plaintiffs' argument, Dr. Nguyen is not inventing a new condition called "physiologic gastroparesis" to describe this presentation. Mot. 4. She instead explains, consistent with Plaintiffs' own experts, that to the extent medication delays gastric emptying, those effects are different from other presentations of gastroparesis because they are generally temporary and

resolve after the patient ceases to take the medication. *See* Nguyen Dep., Ex. D, at 86:14-88:20; Siegel Dep., Ex. H, at 79:2-8; Raines Dep., Ex. I, at 110:15-24, 145:14-25, 265:1-7.

Dr. Nguyen's answer to the Issue 1 question is clear: Reliable diagnoses of "gastroparesis"—whether that term refers to a chronic condition or transient effects—require contemporaneous objective evidence of delayed gastric emptying. The Court should deny Plaintiffs' misplaced request to exclude opinions about whether transient delayed gastric emptying should be called "gastroparesis"—an argument that mischaracterizes Dr. Nguyen's opinions and implicates a dispute that is not before the Court on Issue 1.

II. DR. NGUYEN PROPERLY ADDRESSED IN REBUTTAL AN ABSTRACT THAT PLAINTIFFS' EXPERTS CITED IN THEIR OPENING REPORTS.

As Dr. Nguyen explained in her report, "[t]he premise—underlying the opinions offered by plaintiffs' experts—that symptoms alone are sufficient to diagnose a patient with gastroparesis and/or to establish that they have delayed gastric emptying is false and contradicted by the scientific literature." Nguyen Rpt., Ex. A, at 17. Rather than take issue with Dr. Nguyen's actual conclusion, Plaintiffs focus on a single statement noting that delayed gastric emptying is relatively rare among patients taking a GLP-1RA medication and citing the Lupianez-Merly study as support. *See* Mot. 10-11.

Plaintiffs' attempt to exclude this statement is untenable nitpicking of Dr. Nguyen's rebuttal to the opinions of Dr. Raines and Dr. Siegel, ***who cited in their own reports the very study Dr. Nguyen discussed in her rebuttal***. *See* Raines Rpt., Ex. C, at 12; Siegel Rpt., Ex. B, at 17. Plaintiffs should not question "how [Dr. Nguyen] discovered the Lupianez-Merly abstract," the same abstract cited by their own experts. Mot. 11. The Court can deny Plaintiffs' motion on that basis alone, as it is plainly proper for Dr. Nguyen to consider the materials cited by the experts she rebuts. *See Compl. of Borghese Lane, LLC*, No. 2:18-CV-00533-MJH, 2023 WL 3114851, at *3

(W.D. Pa. Apr. 27, 2023) (collecting cases and observing that expert testimony may "rebut evidence on the same subject matter identified by another party" and "testify as to the flaws that she believes are inherent in another expert's report that implicitly assumes or ignores certain facts" (citations omitted)).

Regardless, Dr. Nguyen properly invoked the Lupianez-Merly abstract to rebut the opinions offered by Dr. Raines and Dr. Siegel. Nguyen Rpt., Ex. A, at 17. Lupianez-Merly found that among a population of 86,682 GLP-1RA users, 14,658 (18%) experienced a gastrointestinal side effect, and 696 were suspected of having delayed gastric emptying. *See* Lupianez-Merly 2024, Ex. P, at 1. Yet only 35% of those 696 actually had delayed gastric emptying when evaluated with objective testing. *Id*. While they hypothesize purported limitations of the study, Plaintiffs' experts concededly identify no data contrary to those presented in Lupianez-Merly and acknowledge that they could cite no evidence indicating that symptoms reliably predict delayed gastric emptying in patients taking GLP-1RAs. *See* Siegel Dep., Ex. H, at 153:25-154:1; Raines Dep., Ex. I, at 251:9-16.

Dr. Nguyen properly considered this abstract in rebutting Plaintiff's experts' opinions and as part of her careful scrutiny of the consistent evidence showing that gastrointestinal symptoms are not a reliable predictor of gastric emptying delay. She did not, as Plaintiffs suggest, offer it as an independent opinion about the effects of GLP-1RA medicines. Plaintiffs' observations about reliability concerns for "unpublished abstracts," Mot. at 11, do not support exclusion either. Dr. Nguyen based her opinions on the extensive literature cited in her report (*e.g.*, Cangemi 2023), her own research (*e.g.*, Pasricha 2011), and the consensus of the leading U.S. and international societies, all of which conclude that symptoms are an unreliable predictor of gastric emptying

delay and cannot be used as a substitute for objective gastric emptying testing. The various sources cited by Dr. Nguyen complement her overarching opinions, including:

- Cangemi 2023, Ex. N at 2671: "Our findings reaffirm guidelines noting that GP cannot be diagnosed based on symptoms alone." *See also* Nguyen Rpt., Ex. A, at 4 ("The Cangemi et al study demonstrates why symptoms cannot reliably be used to diagnose gastroparesis, as such approach was associated with an 80% error rate. . . . Indeed, as illustrated below, numerous physiologic mechanisms—ranging from gastric accommodation and sensation, central nervous system (CNS) processing to psychiatric conditions and small bowel disease—can present with GI symptoms similar to those associated with gastroparesis.").

- Camilleri 2022, Ex. J, at 1202: "Therefore, the presence of [retained gastric food] should not be assumed to be diagnostic of [gastroparesis], and confounding by medications should be excluded in such patients." *See also* Nguyen Rpt., Ex. A, at 11.

- Schol 2025, Ex. G, at 70: International Consensus Guideline noting that "symptoms of gastroparesis lack specificity" and that as a result, "a demonstration of delayed gastric emptying is necessary for diagnosis." *See also* Nguyen Rpt., Ex. A, at 11.

- Parkman 2017, Ex. O, at 10: "In multivariate analysis, [early satiety] but not [postprandial fullness] was associated with impaired gastric emptying." *See also* Nguyen Rpt., Ex. A, at 4 ("In addition to symptoms being non-specific, there is poor correlation between the severity of symptoms and the severity of delayed gastric emptying. Although generally patients with severely delayed gastric emptying are more likely to experience more severe symptoms, there is not always a direct correlation, with some patients experiencing significant symptoms with modest delays while some patients with significant delays experience only minor symptoms.").

- Camilleri 2013, Ex. K, at 19: "Symptoms have not been well correlated with gastric emptying." *See also* Nguyen Rpt., Ex. A, at 10.

- Parkman 2004, Ex. L, at 1592: "Symptoms of gastroparesis are nonspecific and may mimic structural disorders such as ulcer disease, partial gastric or small bowel obstruction, gastric cancer, and pancreaticobiliary disorders"; and "[t]here also is an overlap between the symptoms of gastroparesis and functional dyspepsia." *See also* Nguyen Rpt., Ex. A, at 9.

Moreover, Dr. Nguyen's own research provides addition support for her conclusion. For example, in Pasricha 2011, Dr. Nguyen and her co-authors wrote: "The most important lesson from this multicenter study is that patients with normal gastric emptying and symptoms of nausea and vomiting have a clinical presentation and course that is virtually indistinguishable from those with delayed gastric emptying (i.e. classical gastroparesis)." Pasricha 2011, Ex. M, at 572.

At bottom, Dr. Nguyen did precisely what a rebuttal expert is supposed to do. She "critique[d] [Plaintiffs'] expert[s'] methodologies and point out potential flaws in the experts' reports." *Compl. of Borghese Lane, LLC*, 2023 WL 3114851, at *3 (internal citations and quotations omitted); *see also In re Generic Pharms. Pricing Antitrust Litig.*, No. 16-CB-27242, 2025 WL 478178, at *3 (E.D. Pa. Feb. 12, 2025) (allowing opinions and testimony that "serve to point out issues" "in direct response to [the opponents'] expert reports," to the extent the "opinions are limited to introducing data and evidence that she argues these experts did not properly consider in forming their opinions"). Dr. Nguyen examined and critiqued the literature—including literature cited by Plaintiffs' experts—and tied it to her decades of clinical experience to analyze and respond to Plaintiffs' experts' opinions.

To the extent Plaintiffs contend that Dr. Nguyen did not conduct a literature search, Mot. 6, 11, that is incorrect, as reflected in Dr. Nguyen's report, her materials considered list, and her deposition testimony. *See* Nguyen Rpt., Ex. A, *passim*; Nguyen Rpt., Ex. A, p. 51; Nguyen Dep., Ex. D, at 14:4-24. For example, Plaintiffs suggest that Dr. Nguyen did not do a literature search delineating GLP-1RA-induced delay in gastric emptying and gastroparesis, Mot. 6, but Dr. Nguyen testified that the "the ACG guidelines, the AGA guidelines, the AGA CPU, or the clinical practice updates, the ESNM guidelines, the – it's – all these guidelines from different countries across – you know, within the U.S., in other countries, it accepts that there's a distinction between gastroparesis, the chronic, irreversible disease, and mimickers of gastroparesis that can be reversible." Nguyen Dep., Ex. D, at 91:7-14. To the extent Plaintiffs argue that Dr. Nguyen failed to conduct a literature search on the relationship between GLP-1RAs and gastroparesis, specifically, Mot. 9-11, that is incorrect, too. As Dr. Nguyen explained at her deposition, the scope of the present issue is the reliable diagnosis of gastroparesis, regardless of the cause; not the

magnitude or frequency of gastric emptying delay caused by GLP-1RA medicines. That alone renders Plaintiffs' cases—which are distinguishable on their own terms—inapposite. *See* Mot. 9-10 (quoting, for example, *Espinoza v. Harrelson*, No. 15-CV-1923, 2017 WL 1180012, at *1 (M.D. Fla. Mar. 30, 2017) (ruling that physician-expert could only testify on the plaintiff's injuries from gunshot wounds to the extent his opinion was "drawn from his own, personal evaluation and treatment of plaintiff"), and *Rivlin v. Biomet*, No. 19-CV-1497, 2021 WL 3128672, at *10, 15 (E.D. Pa. July 23, 2021) (striking an airline-expert's opinion about the likelihood of turbulence because, among other reasons, it was based on the pilot's statement about reported turbulence in the area, where expert did not verify the existence of the reports, review the reports, or confirm that the reports actually suggested turbulence existed in the area).

There is no basis for the Court to exclude any of Dr. Nguyen's opinions or statements.

CONCLUSION

For all these reasons, Defendants respectfully request that the Court deny Plaintiffs' motion to partially exclude the opinions of Dr. Linda Nguyen, M.D.

Dated: March 31, 2025

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on March 31, 2025, a true and correct copy of the foregoing Defendants' Joint Response in Opposition to Plaintiffs' Motion to Partially Exclude Opinions of Linda Nguyen, M.D. Under Rule 702 was electronically filed using the Court's CM/ECF System, which will send notification of such filing to all counsel of record.

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